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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,465	06/29/2007	Pascal Perriat	71247-0065	1859

22902 7590 08/02/2010

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EXAMINER	
DO, PENSEE T	
ART UNIT	PAPER NUMBER
1641	
MAIL DATE	DELIVERY MODE
08/02/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,465	PERRIAT ET AL.	
	Examiner	Art Unit	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 May 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *25-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-29* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/29/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

This application 10591465, **PG Pub. No**. 20070281324 filed 06/29/2007 is a national stage entry of PCT/FR05/00491 , International Filing Date: 03/02/2005 and claims foreign priority to 0402115 , filed 03/02/2004. The effective filing date is 3/2/2004.

Election/Restrictions

Applicant's election with traverse of group I, claims 1-24 in the reply filed on May 20, 2010 is acknowledged. The traversal is on the ground(s) that Ponnanpalam (US 2002/0006632) fails to teach coating the polysiloxane coating around the label, landthanide or Europium. This is found persuasive.

However, Applicant's attention is directed to Li et al. (US 2004/0075083).

Li teaches europium-containing fluorescent nanoparticles. The nanoparticle comprises of an aluminum oxide framework having a europium activator and is coated with a polysiloxane coating containing reactive functional groups that allow for attachment of the nanoparticle to a desired biological or chemical agent. (see abstract; [0036]; [[0026]).

Thus, it would have been obvious to one of ordinary skills in the art to coat the hybrid nanoparticles of Bazzi with a polysiloxane as taught by Li for attachment of biological or chemical agent.

Information Disclosure Statement

The IDS submitted on June 29, 2007 has been acknowledged and considered.

Claim Objections

Claim 16 is objected to because of the following informalities: claim 16 recites "Np" twice. Appropriate correction is required.

Claims 5 &6 are objected to because of the following informalities: Claim 6 recites "***fluorescent*** organic molecules" and depends from claim 5 which recites "***luminescent*** organic molecules". Either claim 6 or claim 5 recites a typographical error. Please correct.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131

USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

In the present instance, claim 1 recites the broad recitation 0.5 to 10 nm, and the claim also recites greater than 2 nm and no more than 10 nm which is the narrower statement of the range/limitation.

In the present instance, claim 2 recites the broad recitation 5-75%, and the claim also recites 30-50% which is the narrower statement of the range/limitation.

In the present instance, claim 3 recites the broad recitation 1.6-2.4 and the claim also recites 1.8-2.1 which is the narrower statement of the range.

In the present instance, claims 8 and 9 recite the broad recitation at least 80% by weight (which includes at least 90%), and the claims also recite at least 90% by weight which is a narrower limitation.

In the present instance, claim 16 recites the broad recitation 0.01% to 50%, and the claim also recites 0.1% to 10% which is the narrower statement of the range.

In the present instance, claim 17 recites a broad recitation at least 1% (which includes at least 5%) and the claim also recites at least 5% which is a narrower statement of the limitation.

In the present instance, claim 18 recites the broad recitation 1 to 1000, and the claim also recites 1 to 100 which is the narrower statement for the range.

In the present instance, claim 23 recites the broad recitation of less than 5000 g/mol, and the claim also recites less than 1000 which is the narrower statement of the limitation.

Regarding claim 17, the phrase "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 7-15, 18-22, 24 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12, 14-16, 19-22, 24 and 31 of copending Application No. 12/293,486 (***copending appl. '486***) in view of Li et al (US 2004/0075083).

Copending appl. '486 claims nanoparticles comprising a core and shell structure, wherein the core is made up of rare earth metal oxide such as europium and a coating of thickness between 1-10 nm.

However, copending appl. '486 fails to teach a polysiloxane coating and at least one biological ligand grafted by covalent bonding to the polysiloxane coating.

Li teaches Europium (Eu)-containing fluorescent nanoparticles comprising an aluminum oxide framework having Europium activator, and at least one energy reservoir selected from Mg, Ca, Sr and Ba and one co-activator such as Sc, Y, La, Ce, Pr, Nd, etc...(see [0006]). The nanoparticles are coated with a silicon-containing compound such as siloxane or polysiloxane which contains functional groups through which biological molecules such as proteins, nucleic acids, carbohydrate are bound (see [0036], [0026]).

Therefore, it would have been obvious to one of ordinary skill in the art to coat the nanoparticle copending appl. '486 with a functionalized polysiloxane coating as taught by Li so that the nanoparticles of copending appl. '486 can be used as labels in

biological assays. One of ordinary skill in the art would have a reasonable expectation of success when combining the teachings of Li and copending appl. '486 because both teach using nanoparticles that are doped with rare earth elements such as Europium.

This is a provisional obviousness-type double patenting rejection.

Claims 5 and 6 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12, 14-16, 19-22, 24 and 31 of copending Application No. 12/293,486 (***copending appl. '486***) in view of Li et al (US 2004/0075083) as applied to claim 1 above, and further in view of Yates et al. (US 4,921,589).

Copending appl. '486 and Li have been discussed above.

However, they fail to teach covalently attaching 100 to 1000 molecules of organic fluorescent molecules to the coating of the nanoparticles and such organic fluorescent molecules are fluorescein or rhodamine.

Yates teaches applying a coating of polysiloxanes onto a substrate such as spheres or glass spheres (see col. 7, lines 10-22); Then applying a solution of photosensitizers such as fluorescein or rhodamine onto the polysiloxane coating. (see col. 4, line 50-col. 5, lines 13). Yates teaches the coating of polysiloxane of formula I, II or III on col. 5, line 43-col. 6,line 39) with m or n being integers of 200-2000 which represents how many molecules of siloxanes in the polysiloxane. Thus, when the photosensitizers are coated onto the polysiloxane, they would bind through the O-Si bond or C-Si bond of the polysiloxane (see col. 5,lines 13-16) and thus since there are

200-2000 siloxanes or O-Si or C-Si bonds are available, 200-2000 of organic fluorescent molecules would bind. The photosensitizer produces singlet oxygen which has a long enough lifetime to be chemically active in solution. The singlet oxygen is also a stronger oxidizing agent (see col. 1,lines 5-17).

Thus, one of ordinary skill in the art would have been covalently attach Rhodamine or Fluorescein onto polysiloxane coating of the nanoparticles in copending appl. '486 modified with Li by the method taught by Yates since these photosensitizers produce singlet oxygen which is a stronger oxidizing agent. One of ordinary skill in the art would have a reasonable expectation of success in combining these teachings since they all teach using polysiloxane coating on spheres.

This is a provisional obviousness-type double patenting rejection.

Claim 16 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12, 14-16, 19-22, 24 and 31 of copending Application No. 12/293,486 (***copending appl. '486***) in view of Li et al (US 2004/0075083) as applied to claim 1 above, and further in view of O'Beirne (US 7,101,719 filed on Nov. 5, 2001).

Copending appl. '486 and Li have been discussed above.

However, they fail to teach 0.01% to 50 % of the metal cations of the nanosphere are uranide cations chosen from Ac, Th, Pa, Np, U, Pu.

O'Beirne teaches doping an inorganic host material such as ytrrium oxide (see col. 6, lines 1-15) with an activator such as uranium. (see col. 6, lines 14-30).

Since it is well known in the art uranium can be used as an activator for doping inorganic host material such as yttrium oxide beside terbium, europium, erbium, etc, it would have been obvious to one of ordinary skill in the art to add uranium to yttrium oxide of copending appl. '486 modified with Li to obtain nanoparticles doped with rare earth metal cations such as uranium to produce a nanoparticle with a unique emission spectrum distinguished from the other nanoparticles doped with a different activator. One of ordinary skill in the art would have a reasonable expectation of success in combining these teachings since they all teach doping nanoparticles with rare earth metal cations.

This is a provisional obviousness-type double patenting rejection.

Claims 17 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12, 14-16, 19-22, 24 and 31 of copending Application No. 12/293,486 (***copending appl. '486***) in view of Li et al (US 2004/0075083) as applied to claim 1 above, and further in view of Kresse et al. (US 5,427,767).

Copending appl. '486 and Li have been discussed above.

However, they fail to teach adding U^{235} or Gd^{157}.

Kresse teaches that: "Another possible approach to therapy can be taken by insertion of ^{57}Co into ferrites and accomplishing neutron activation for thermal and epithermal neutrons taking advantage of the large capture cross section of ^{57}Co. As in resonant nuclear absorption through photons (Mossbauer) described above, tissue

containing no 157Gd will scarcely take up neutrons and consequently will not be detrimentally affected. Neutron uptake is primarily concentrated on the areas containing 157Gd. Hence, sufficient enrichment of the tumor provided, radiation damage is inflicted only on the tumor by secondary radiation (Auger electrons and photons). The particles must be doped with the appropriate isotopes for application of ferrite/magnetite in therapy. (see col. 5, lines 34-45).

Since Kresse teaches doping magnetic nanoparticles with 157Gd for application in cancer therapy, it would have been obvious to ordinary skill in the art to incorporate Gd157 as an activator or dopant into the magnetic host of copending appl. '486 modified with Li to obtain nanoparticles doped with Gd157 for use in cancer therapy. One of ordinary skill in the art would have a reasonable expectation of success in combining these teachings because they all teach using Gd as a dopant in magnetic hosts, i.e. Y2O3.

This is a provisional obviousness-type double patenting rejection.

Claim 23 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12, 14-16, 19-22, 24 and 31 of copending Application No. 12/293,486 (***copending appl. '486***) in view of Li et al (US 2004/0075083) as applied to claim 1 above, and further in view of Molina et al. (Chem. Mater. 2001, 13, 2818-2823).

Copending appl. '486 and Li have been discussed above.

However, they fail to teach a water-soluble polymer such as dextran or polyethylene glycol is grafted onto the coating of the nanoparticle.

Molina teaches mixing polyethylene glycol with siloxane to coat Eu3+ and such coating offers high visible transparency, flexibility and good chemical stability. When these materials contain Europium ions, potentially interesting phosphor are obtained. The nature of the Eu3+ first coordination shell in these hybrids of polyethylene and siloxane may be tuned, as a function of both the salt concentration and the polymer molecular weight. (see entire document especially pg. 2818, col. 2).

Thus, it would have been obvious to one of ordinary skill in the art to combine polyethylene glycol and siloxane or polysiloxane as the coating to coat Eu3+ to obtain nanoparticles with a shell of high visible transparency, flexibility and good chemical stability (see Molina p. 2818, col.2) as taught by Molina. One of ordinary skills in the art would have a reasonable expectation of success in combining the teachings of Molina with copending appl. '486 modified with Li since they all teach using nanoparticles doped with Europium ions.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 7-15, 18-22, 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bazzi et al. (Journal of Luminescence 102-103 (2003) p. 445-450 submitted by applicants) in view of Li et al. (US 2004/0075083) and Baumann et al. (US 6,099,964).

Bazzi teaches a highly luminescent hybrid nanoparticle comprising a nanosphere of diameter from 2-5 nm (see abstract), of which at least 90% by weight consists of sesquioxides Ln2O3 and doped Ln3+ yttrium or gadolinium oxides (Ln=Eu, Tb, Nd, Gd, or Y) (which are rare earth elements) (see entire document especially p. 446, col. 2, 1st paragraph and p. 450).

However, Bazzi fails to teach that the nanoparticle has a polysiloxane coating having a mean thickness within the range from 0.5 to 10 nm; and at least one biological ligand grafted by covalent bonding to the polysiloxane coating.

Li teaches Europium (Eu)-containing fluorescent nanoparticles comprising an aluminum oxide framework having Europium activator, and at least one energy reservoir selected from Mg, Ca, Sr and Ba and one co-activator such as Sc, Y, La, Ce, Pr, Nd, etc...(see [0006]). The nanoparticles are coated with a silicon-containing compound such as siloxane or polysiloxane which contains functional groups through which biological molecules such as proteins, nucleic acids, carbohydrate are bound (see [0036], [0026]).

Therefore, it would have been obvious to one of ordinary skill in the art to coat the nanoparticle of Bazzi with a functionalized polysiloxane coating as taught by Li so

that the nanoparticles of Bazzi can be used as labels in biological assays. One of ordinary skill in the art would have a reasonable expectation of success when combining the teachings of Li and Bazzi because both teach using nanoparticles that are doped with rare earth elements such as Europium.

However, Bazzi and Li fail to teach the polysiloxane layer has a thickness between 0.5 to 10 nm.

Baumann et al. teach organopolysiloxane particles which have an average diameter of 5-200 nm. The particles have a siloxane shell with a thickness of 1 to 100 nm. (see abstract; col. 5, lines 18-19).

Since it is well known in the art that polysiloxane coating with a thickness of 1-100 nm are used to obtain particles with average size of 5-200 nm as taught by Baumann, it would have been obvious to one of ordinary skill in the art to coat the particles of Bazzi and Li with a thickness of 2-100 nm to obtain particles size of 5-200 nm in order to completely cover the core. One of ordinary skill in the art would have a reasonable expectation of success in combining the teachings of Bazzi, Li and Baumann since they all teach obtaining nanoparticles with average size of 5 nm.

For claim 2, since Li teaches the same polysiloxane coating as that of the present invention, 5 to 75 % of the silicon atoms must be bound to four other silicon atoms by oxygen bridges in such polysiloxane taught by Li.

For claims 3 and 4, since Li teaches the same polysiloxane coating as that of the present invention, such polysiloxane coating in Li must have a density of 1.6 to 2.4 or less than 2.

For claim 7, Bazzi teaches that the nanoparticles contain at least 80% by weight of a rare earth sesquioxides (see entire document especially p. 446, col. 2, 1st paragraph and p. 450).

For claims 8 and 9, Bazzi teaches that the nanosphere, for at least 80% by weight, consists of Gd2O3 or Y2O3. (see entire document especially p. 446, col. 2, 1st paragraph and p. 450).

For claim 10, Bazzi teaches the nanosphere is doped with a lanthanide of type Eu, Tb, Er, Nd, Yb representing from 0.1 to 25% of the metal cations. (see entire document especially p. 446, col. 2, 1st paragraph and p. 450; pp. 447 results and discussion).

For claims 11, 12, 14 and 15, Bazzi teaches that the nanosphere is doped with a lanthanide of type Nd or Yb, or Er. (see entire document especially p. 446, col. 2, 1st paragraph and p. 450; pp. 447 results discussion).

For claim 13, Bazzi teaches the nanosphere is doped with at least two different lanthanides representing from 0.1 to 25% of the metal cations, at least one of these is Eu, i.e. Y2O3:Eu (see entire document especially p. 446, col. 2, 1st paragraph and p. 450; pp. 447 results discussion).

For claim 18, Li teaches coating the nanoparticle with polyclonal antibody. (see [0056]).

For claim 19, Li teaches that the coating composition of the nanoparticle has one or more functional groups and these functional groups are used to link biological molecules onto the particles. (see [0036]). Thus, it would have been obvious to one of

ordinary skill in the art that those nanoparticles which are coated with a coating having two functional groups would be bound to two different biological molecules.

For claim 20, Li teaches the grafted biological ligand is a carbohydrate. (see [039]).

For claim 21, Li teaches the nanoparticles are bound to small molecules (complexing molecules) other than biological molecules. (see [0036]).

For claim 22, Li teaches phosphate (organophosphate) or DNA, RNA (also an organophosphate) is grafted onto the coating. (see [0036]).

For claim 24, Bazzi teaches the colloidal suspension of the hybrid nanoparticles. (see p. 446, col. 2, first paragraph).

Claims 5, 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bazzi in view of Li and Baumann as applied to claim 1 above, and further in view of Yates et al. (US 4,921,589).

Bazzi, Li and Baumann have been discussed above.

However, they fail to teach covalently attaching 100 to 1000 molecules of organic fluorescent molecules to the coating of the nanoparticles and such organic fluorescent molecules are fluorescein or rhodamine.

Yates teaches applying a coating of polysiloxanes onto a substrate such as spheres or glass spheres (see col. 7, lines 10-22); Then applying a solution of photosensitizers such as fluorescein or rhodamine onto the polysiloxane coating. (see col. 4, line 50-col. 5, lines 13). Yates teaches the coating of polysiloxane of formula I, II

or III on col. 5, line 43-col. 6,line 39) with m or n being integers of 200-2000 which represents how many molecules of siloxanes in the polysiloxane. Thus, when the photosensitizers are coated onto the polysiloxane, they would bind through the O-Si bond or C-Si bond of the polysiloxane (see col. 5,lines 13-16) and thus since there are 200-2000 siloxanes or O-Si or C-Si bonds are available, 200-2000 of organic fluorescent molecules would bind. The photosensitizer produces singlet oxygen which has a long enough lifetime to be chemically active in solution. The singlet oxygen is also a stronger oxidizing agent (see col. 1,lines 5-17).

Thus, one of ordinary skill in the art would have been covalently attach Rhodamine or Fluorescein onto polysiloxane coating of the nanoparticles in Bazzi modified with Li and Baumann by the method taught by Yates since these photosensitizers produce singlet oxygen which is a stronger oxidizing agent. One of ordinary skill in the art would have a reasonable expectation of success in combining these teachings since they all teach using polysiloxane coating on spheres.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bazzi in view of Li and Baumann as applied to claim 1 above, and further in view of O'Beirne (US 7,101,719 filed on Nov. 5, 2001).

Bazzi, Li and Baumann have been discussed above.

However, they fail to teach 0.01% to 50 % of the metal cations of the nanosphere are uranide cations chosen from Ac, Th, Pa, Np, U, Pu.

O'Beirne teaches doping an inorganic host material such as ytrrium oxide (see col. 6, lines 1-15) with an activator such as uranium. (see col. 6, lines 14-30).

Since it is well known in the art uranium can be used as an activator for doping inorganic host material such as yttrium oxide beside terbium, europium, erbium, etc, it would have been obvious to one of ordinary skill in the art to add uranium to yttrium oxide of Bazzi and modified with Li and Baumann to obtain nanoparticles doped with rare earth metal cations such as uranium to produce a nanoparticle with a unique emission spectrum distinguished from the other nanoparticles doped with a different activator. One of ordinary skill in the art would have a reasonable expectation of success in combining these teachings since they all teach doping nanoparticles with rare earth metal cations.

Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bazzi in view of Li and Baumann as applied to claim 1 above, and further in view of Kresse et al. (US 5,427,767).

Bazzi, Li and Baumann have been discussed above.

However, they fail to teach adding U^{235} or Gd^{157}.

Kresse teaches that: "Another possible approach to therapy can be taken by insertion of ^{157}Gd into ferrites and accomplishing neutron activation for thermal and epithermal neutrons taking advantage of the large capture cross section of ^{157}Gd. As in resonant nuclear absorption through photons (Mossbauer) described above, tissue containing no ^{157}Gd will scarcely take up neutrons and consequently will not be

detrimentally affected. Neutron uptake is primarily concentrated on the areas containing 157Gd. Hence, sufficient enrichment of the tumor provided, radiation damage is inflicted only on the tumor by secondary radiation (Auger electrons and photons). The particles must be doped with the appropriate isotopes for application of ferrite/magnetite in therapy. (see col. 5, lines 34-45).

Since Kresse teaches doping magnetic nanoparticles with 157Gd for application in cancer therapy, it would have been obvious to ordinary skill in the art to incorporate Gd157 as an activator or dopant into the magnetic host of Bazzi modified with Li and Baumman to obtain nanoparticles doped with Gd157 for use in cancer therapy. One of ordinary skill in the art would have a reasonable expectation of success in combining these teachings because they all teach using Gd as a dopant in magnetic hosts, i.e. Y2O3.

Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bazzi in view of Li and Baumann as applied to claim 1 above, and further in view of Molina et al. (Chem. Mater. 2001, 13, 2818-2823).

Bazzi, Li and Baumann have been discussed above.

However, they fail to teach a water-soluble polymer such as dextran or polyethylene glycol is grafted onto the coating of the nanoparticle.

Molina teaches mixing polyethylene glycol with siloxane to coat Eu3+ and such coating offers high visible transparency, flexibility and good chemical stability. When

these materials contain Europium ions, potentially interesting phosphor are obtained. The nature of the Eu3+ first coordination shell in these hybrids of polyethylene and siloxane may be tuned, as a function of both the salt concentration and the polymer molecular weight. (see entire document especially pg. 2818, col. 2).

Thus, it would have been obvious to one of ordinary skill in the art to combine polyethylene glycol and siloxane or polysiloxane as the coating to coat Eu3+ to obtain nanoparticles with a shell of high visible transparency, flexibility and good chemical stability (see Molina p. 2818, col.2) as taught by Molina. One of ordinary skills in the art would have a reasonable expectation of success in combining the teachings of Molina with Bazzi modified with Li and Baumann since they all teach using nanoparticles doped with Europium ions.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Pensee T. Do/
Examiner, Art Unit 1641

/Jacob Cheu/
Primary Examiner, Art Unit 1641